

REMARKS

This application is amended in a manner to place it in condition for allowance at the time of the next Official Action.

**Status of the Claims**

Claims 21, 22, 25, 32, 33, 38 and 39 are amended. Support for the amendment to the claims may be found, for example, at page 4, lines 8-27, page 10, lines 1-2, page 14, lines 14-17, and page 15, lines 16-19.

Claims 21-40 remain in this application.

**Claim Rejections-35 USC §112**

Claims 25, 39 and 40 were rejected under 35 U.S.C. §112, second paragraph, for being indefinite. This rejection is respectfully traversed for the reasons below.

Specifically claim 25 was rejected for reciting a polymer molecular weight, but the composition of polymer is not specified. However, claim 21 has amended to recite that the organic phase comprises a biodegradable polymer, and, thus, claim 25 refers to this polymer.

Claims 39 and 40 were rejected because claim 39 recited a use without a process step, but claim 39 has been amended to recite the step of "administering".

Therefore, withdrawal of the rejection is respectfully requested.

**Claim Rejections-35 USC §101**

Claims 39 and 40 were rejected under 35 U.S.C. §101 for reciting a use. As claim 39 has been amended to recite an active step instead of a use, withdrawal of the rejection is respectfully requested.

**Claim Rejections-35 USC §103**

Claims 21-38 were rejected under 35 U.S.C. §103(a) as being unpatentable over BIBETTE, et al. US 5,938,581 (BIBETTE) in view of OKADA, et al. US 5,643,607 (OKADA) and LOBO, et al. US 5,589,332 (LOBO). This rejection is respectfully traversed for the reasons below.

**The claimed invention**

The claimed method is directed to preparing monodisperse biodegradable microspheres, which includes the step of preparing an emulsion from at least one organic phase with an active ingredient and a biodegradable polymer dissolved in an organic solvent, and at least one aqueous phase, the viscosity of the organic phase and the aqueous phase having a ratio of from 0.1 to 10. After preparing the emulsion it is subjected to controlled laminar shearing, the solvent is removed from the organic phase, and the microspheres obtained are isolated.

BIBETTE

BIBETTE describes a method for the preparation of double emulsions by subjecting a controlled laminar shear to a primary emulsion, such that the same maximum shear is applied to the entire emulsion. In particular, the shear conditions are obtained in a coquette cell. See, e.g., Figure 1, column 5, line 59.

As acknowledged in the Official Action, BIBETTE discloses oil-in-water emulsions containing an active ingredient.

However, as further acknowledged in the Official Action, BIBETTE does not disclose emulsions comprising biodegradable polymers.

The Official Action further referred to specific oils according to BIBETTE at column 2, lines 28-60, and the use of silicone polymers suggested at column 2, line 41 of BIBETTE.

However, in column 2, BIBETTE discloses that oils of the emulsions may be polymers such as polyacrylic acid (line 33) or polyorganosiloxanes (line 36). However, these polymers are not biodegradable polymers.

Furthermore, the Official Action correlated the viscoelastic property of the emulsion of BIBETTE to a ratio of the viscosity of the organic phase and the aqueous phase of 0.1 to 10, as recited in claim 21 of the present invention. This correlation was based on the range of 0.1 to 10 for the values of

G' and G'' as taught by BIBETTE in equation 4 of column 3, line 65.

However, there is no suggestion in BIBETTE that the values of G' and G'' are linked to the ratio of the viscosity of the organic phase and the aqueous phase.

OKADA

OKADA fails to remedy the deficiencies of BIBETTE for reference purposes.

OKADA describes a process for making a direct dispersion of a photographically useful material without the use of auxiliary solvents. The ratio of the organic phase viscosity to the aqueous phase viscosity (i.e., a gelatine solution viscosity) is disclosed as greater than 2 (column 4, lines 39-42) to obtain a fine dispersion.

However, this teaching is given only for a process with high shear such as an example with a Brinkmann rotor starter device (column 15, line 14) followed by a homogenization step.

The mean dispersion particle size is indeed low (less than  $0.5\mu$ ) (table in column 16), but there is no indication from OKADA suggesting that it relates to monodisperse emulsions.

Accordingly, one of ordinary skill in the art would not have considered OKADA as relating to monodisperse emulsions.

LOBO

LOBO also fails to remedy the deficiencies of BIBETTE as well as the combination of BIBETTE and OKADA for reference purposes.

LOBO discloses microcapsules for sustained release of hydrophilic active substances, in particular peptides. These microcapsules are prepared by subjecting an emulsion to microencapsulation, wherein the emulsion has a dispersed aqueous phase containing active substances and a continuous phase containing polymers.

This document is cited and discussed in the present application.

Most significantly, LOBO describes microspheres wherein the release kinetics of the active substance is non-homogenous, as the microspheres have a broad particle size distribution. As a result, are not monodisperse microspheres.

Therefore, the proposed combination fails to disclose or suggest the claimed invention, and withdrawal of the rejection is respectfully requested.

Conclusion

In view of the amendment to the claims and the foregoing remarks, this application is in condition for allowance at the time of the next Official Action. Allowance and passage to issue on that basis is respectfully requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future submissions, to charge any deficiency or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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